REMARKS

Claims 75-129 are pending in the present application. By virtue of this response, claims 105 and 124 have been cancelled, claims 90, 93-94, 111, and 113 have been amended, and no new claims have been added. Accordingly, claims 75-104, 106-123, and 125-129 are currently under consideration.

The amendments to claims 90 and 111 can be found, *inter alia*, at page 7, line 28 to page 8, line 1 of the specification, as well as in previously pending claims 105 and 124. The amendments to claims 93-94 and 113 can be found, *inter alia*, at page 8, line 17 to page 9, line 4, of the specification.

With respect to claim amendments and cancellation, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional applications.

Claim Interpretation

The Examiner maintains that the recitation of the term "about" in the pending claims allows for a broad interpretation of dose ranges and that the claims therefore encompass any percentage of any conventional dose of paclitaxel as long as the dose is functional for its intended purpose. Applicants respectfully disagree.

Without acquiescing to the Examiner's assertions and solely in the interest of expediting prosecution, claims 90, 93, 94, 111, and 113 have been amended to delete the term "about."

Claim Rejections – 35 USC § 112, Second Paragraph

Claims 90-129 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. According to the Examiner, there is insufficient antecedent basis for "the conventional

dose of paclitaxel" in claims 90 and 111 and their dependent claims; and that the claims can be interpreted to encompass any percentage of any conventional dose of paclitaxel for chemotherapy. The Examiner further states that claims 90-129 are unclear with respect to whether the claimed dose ranges (e.g., about 1% to about 10%) of the conventional dose of paclitaxel over the same period are cumulative doses or individual doses.

Solely in an effort to expedite prosecution and without acquiescing to the Examiner's rejection, claims 90 and 111 have been amended to recite that the amount of paclitaxel is "1% to 20% of a conventional dose of paclitaxel over the same period . . . wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks," or "1% to 10% of a conventional dose of paclitaxel over the same period, wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks," respectively. Support for the claim amendment can be found, *inter alia*, at page 7, line 28 to page 8, line 1, of the specification. Accordingly, the 35 U.S.C. § 112 rejection is obviated by the claim amendment.

Applicants respectfully submit that one of ordinary skill in the art reading the claims will readily understand that the claimed "1% to 20% of a conventional dose" or "1% to 10% of a conventional dose" refer to a cumulative dose over the same period. For example, in a three week period, the total amount of paclitaxel administered to the individual is 1% to 20% (or 1% to 10%) of the conventional dose of 135-175 mg/m^2.

Applicants respectfully request that the rejection of claims 90-129 under 35 U.S.C. § 112 be withdrawn.

Claim Rejections – 35 USC § 112, First paragraph

Claims 75-89

Claims 75-89 and their dependent claims 76-89 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleges that the specification provides no description of any specific doses, administration routes, or

administration regimens that would result in maintenance of the claimed plasma level of paclitaxel over a period of 7 days or more. Applicants respectfully traverse.

As stated in the Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1, "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." "Written Description" Requirement, Federal Register, Vol. 66, No. 4, p. 1106, Friday, January 5, 2001.

Applicants respectfully submit that claim 75 provides specific plasma concentrations to be reached in the claimed method of administration. Because pharmacokinetic parameters of paclitaxel (e.g. volume of distribution, clearance, and half life) are known in the art (see, e.g. Exhibit I, Goodman & Gilman's The Pharmacological Basis of Therapeutics, 1260-1261 and 1768-1769 (Joel Hardman, ed., McGraw-Hill 1996) (1941)), one skilled in the art can calculate an appropriate dose and a dosing interval to achieve a steady-state concentration of paclitaxel in plasma. ("If the clinician choose the desired concentration of drug in plasma and knows the clearance and availability for that drug in a particular patient, the appropriate dose and dosing interval can be calculated"). Exhibit II, Goodman & Gilman's The Pharmacological Basis of Therapeutics, 24 (Joel Hardman, ed., McGraw-Hill 1996) (1941)). Accordingly, given a specified plasma level of paclitaxel as claimed herein, one skilled in the art can determine the appropriate dosage of paclitaxel for any route or formulation in order to reach the claimed plasma level. Thus, one of ordinary skill in the art would have understood the inventors to be in possession of the claimed invention.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 90-129

Claims 90-129 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleges that there is no written

basis for the claimed conventional dose of paclitaxel or amounts of paclitaxel that can be administered over a period of 7 days or more. Applicants respectfully traverse this rejection.

As discussed above, solely in an effort to expedite prosecution of this case, claims 90 and 111 have been amended to recite that the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks. Accordingly, Applicants respectfully submit that the amendment obviates the rejection under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be withdrawn.

Claim Rejections – 35 USC § 102(b)

Chang et al.

Claims 90-91, 93-95, 97-98, 100, 103, 105-114, 116-117, 119, 122, and 124-129, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chang et al. ("Chang"). The Examiner alleges that the claims encompass administering a dose of paclitaxel that is "any" percentage of any conventionally administered dose of paclitaxel as long as such dose is functional for its intended purpose and also states that "in the absence of evidence to the contrary, the Examiner is not persuaded that administration of 50 mg/m^2/week paclitaxel will not result in a therapeutically effective plasma level of paclitaxel throughout the period of 7 days or more as instantly claimed." Applicants respectfully traverse this rejection.

The Examiner's rejection is based on the broad interpretation of the term "about" when making the rejection. Applicants respectfully disagree with this interpretation which relies on the term "about" to reach an entire range of values, which is contrary to a reasonable interpretation of this term. However, as discussed above, independent claims 90 and 111 have been amended to recite that the amount of paclitaxel is "1% to 20%" or "1% to 10%"of the conventional dose of paclitaxel over a period of 7 days or more, "wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks." Thus, the Examiner's rational is inapplicable to the amended claims. As currently amended, 1% up to 20% of the conventional dose of paclitaxel in the

concentration is well below the starting dose of 50 mg/m^2/week paclitaxel in the dose escalation study disclosed in Chang.

Furthermore, with respect to claims 90, 111, and their dependent claims, Applicants respectfully submit that Chang is completely silent about maintaining a therapeutically effective plasma level of paclitaxel throughout the period of 7 days or more using the dose range as recited in amended claim 90 or regularly administering paclitaxel over a period of 7 days or more using the dose range as recited in amended claim 111.

Applicants therefore respectfully request that the rejection based on Chang be withdrawn.

Klaassen et al.

Claims 90-95, 97-98, 100, 103, 105-108, 110-114, 116-117, 119, 122, 124-127, and 129, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Klaassen et al. ("Klaassen"). The Examiner alleges that the claims reasonably encompass administering a dose of paclitaxel that is "any" percentage of any conventionally administered dose of paclitaxel as long as such dose is functional for its intended purpose and also states that "in the absence of evidence to the contrary, the Examiner is not persuaded that administration of the doses of paclitaxel taught in Klaassen will not result in a therapeutically effective plasma level of paclitaxel throughout the period of 7 days or more as instantly claimed." Applicants respectfully traverse this rejection.

The Examiner's rejection is based on the broad interpretation of the term "about" when making the rejection. As discussed above, claims have been amended to recite that the amount of paclitaxel is "1% to 20%" or "1% to 10%"of the conventional dose of paclitaxel over a period of 7 days or more, "wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks." Thus, Examiner's rational is inapplicable. Klaassen discloses administration of paclitaxel via a 1-hour infusion on days 1, 8, 15, 22, 29, and 36 (every 50 days) at dose levels of 70 mg/m^2/wk, 80 mg/m^2/wk, 90 mg/m^2/wk, and 100 mg/m^2/wk. As currently amended, claims 90, 111, and their dependent claims recite a range of dose levels that is well below the dose levels as disclosed in Klassen.

Furthermore, with respect to claims 90, 111, and their dependent claims, Applicants respectfully submit that Klaassen is completely silent about maintaining a therapeutically effective plasma level of paclitaxel throughout the period of 7 days or more using the dose levels as recited in amended claim 90 or regularly administering paclitaxel over a period of 7 days or more using the dose levels as recited in amended claim 111.

Applicants therefore respectfully request that the rejection based on Klaassen be withdrawn.

Fennelly et al.

Claims 90-95, 97-98, 100, 103, 105-108, 110-114, 116-117, 119, 122, 124-127, and 129, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Fennelly et al. ("Fennelly"). The Examiner alleges that the claims reasonably encompass administering a dose of paclitaxel that is "any" percentage of any conventionally administered dose of paclitaxel as long as such dose is functional for its intended purpose and also states that "in the absence of evidence to the contrary, the Examiner is not persuaded that administration the doses of paclitaxel taught in Fennelly will not result in a therapeutically effective plasma level of paclitaxel as instantly claimed." Applicants respectfully traverse this rejection.

The Examiner's rejection is based on the broad interpretation of the term "about" when making the rejection. As discussed above, claims have been amended to recite that the amount of paclitaxel is "1% to 20%" or "1% to 10%"of the conventional dose of paclitaxel over a period of 7 days or more, "wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks." Fennelly teaches escalating-doses of paclitaxel at 40 mg/m^2/wk, 50 mg/m^2/wk, 60 mg/m^2/wk, 80 mg/m^2/wk, and 100 mg/m^2/wk administered as a 1-hour infusion in patients with recurrent ovarian cancer. As currently amended, claims 90, 111, and their dependent claims, recite a range of dose levels that is well below the dose levels as disclosed in Fennelly.

Furthermore, with respect to claims 90, 111, and their dependent claims, Applicants respectfully submit that Fennelly is completely silent about maintaining a therapeutically effective plasma level of paclitaxel throughout the period of 7 days or more using the dose levels as recited in

amended claim 90 or regularly administering paclitaxel over a period of 7 days or more using the dose levels as recited in amended claim 111.

Applicants therefore respectfully request that the rejection based on Fennelly be withdrawn.

Claim Rejections – 35 USC § 103(a)

Fennelly et al. in view of WO98/14174

Claims 99, 101, 118, and 120, stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fennelly as applied to claims 90-95, 97-98, 100, 103, 105-108, 110-114, 116-117, 119, 122, 124-127, and 129 above, and further in view of WO 98/14174 ("WO '174"). Applicants respectfully disagree.

Applicants will address this rejection as it might apply to amended claims. As discussed above, Fennelly does not teach or suggest administering paclitaxel at 1% to 20% (or 1% to 10%) of the conventional dose of paclitaxel over a period of 7 days or more, wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks, as recited in the presently amended claims.

WO'174 does not cure the deficiencies of Fennelly. Specifically, WO '174 is cited as allegedly disclosing compositions and methods useful for the *in vivo* delivery of substantially insoluble pharmacologically active agents in the form of suspended particles coated with a protein or in the form of a redispersible dry powder comprising nanoparticles of water-insoluble drug coated with a protein. WO '174 does not teach or suggest administering paclitaxel at 1% to 20% (or 1% to 10%) of the conventional dose over a period of 7 days or more as recited in the presently amended claims.

Accordingly, Applicants respectfully submit that neither Fennelly nor WO'174 application, alone or in combination, discloses the claimed methods and renders the dosing regimen as currently claimed obvious to one skilled in the art.

Fennelly et al. in view of U.S. 6,211,171

Claims 99-104 and 118-123 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fennelly as applied to claims 90-95, 97-98, 100, 103, 105-108, 110-114, 116-117, 119, 122, 124-127, and 129 above, and further in view of U.S. Patent No. 6,211,171 (U.S. '171). Applicants respectfully traverse the rejection.

Applicants will address this rejection as it might apply to amended claims. As discussed above, Fennelly does not teach or suggest administering paclitaxel at 1% to 20% (or 1% to 10%) of the conventional dose of paclitaxel over a period of 7 days or more, wherein the conventional dose of paclitaxel is 135-175 mg/m^2 over a period of three weeks, as recited in the presently amended claims.

U.S. '171 does not cure the deficiencies of Fennelly. Specifically, US '171 is cited as allegedly disclosing compositions formulated for local injections comprising a physiological compatible saline solution and may optionally be encapsulated in a slow release delivery vehicle, including a colloidal dispersion system (*e.g.* nanocapsules) or in polymer stabilized crystals. *See* col. 11, lines 1-17. US '171 does not teach or suggest administering paclitaxel at 1% to 20% (or 1% to 10%) of the conventional dose over a period of 7 days or more as recited in the present claims.

Accordingly, Applicants respectfully submit that neither Fennelly nor U.S. '171 application, alone or in combination, discloses the claimed methods and renders the dosing regimen as currently claimed obvious to one skilled in the art.

Double Patenting Rejection

Claims 90-98, 105-117, and 124-129, stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-14 of copending Application No. 11/644,850. Applicants again respectfully request that this provisional rejection be held in abeyance until the Office has made determination of otherwise allowable claims in the present application or co-pending application No. 11/644,850.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 638772000200. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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